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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,634	02/19/2002	Paul Habermann	02481.1774	2606

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EXAMINER	
DUFFY, PATRICIA ANN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 05/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,634	HABERMANN ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 2-27-06.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-5,9-14,16-21 and 23 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-5,9-14,16-21 and 23 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2-27-06 has been entered.

The amendment filed 2-27-06 has been entered into the record. Claims 6-8, 15, 22 and 24-25 have been cancelled. Claims 1-5, 9-14, 16-21 and 23 are pending and under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Election/Restrictions

The election/restriction is moot in view of the cancellation of the non-elected subject matter.

Rejections Withdrawn

Claim 1-6 and 9-23 of this application conflict with claims 1-3 and 7-20 of Application No. 10/076,631 and claims 1-3 and 7-20 of Application No. 10/076,632 is withdrawn in view of Applicants amendments and arguments.

The rejection of the claims 1-5, 9-14, 16-21 and 23 as rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn over the issue of signal sequence in view of arguments and in view of the amendments to claim 17 only.

The rejection of claims 1, 2, 6, 9-15, 17, 22 and 23 under 35 U.S.C. 102(b) as being clearly anticipated by Dawson et al, WO 91/09125 published 27 June 1991 is withdrawn in view of the amendments to the claims.

The rejection of claims 1-5, 9-14, 16-21 and 23-25 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as set forth as a new rejection at page 9 of the last office action is withdrawn in view of the amendments to the claims.

Rejections Maintained

Claims 1-5, 9-14, 16-21 and 23 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 7-20 of copending Application No. 10/076,631. Although the conflicting claims are not identical, they are not patentably distinct from each other because the specifically claimed and disclosed species anticipate the instantly claimed invention is maintained for reasons made of record in the office action mailed 6-16-04.

Applicants' arguments and amendments are noted but still do not obviate the rejection of record. The rejection is maintained for reasons made of record until all the claims are rendered allowable.

Claims 1-5, 9-14, 16-21 and 23 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 7-20 of copending Application No. 10/076,632. Although the conflicting claims are not identical, they are not patentably distinct from each other because the specifically claimed and disclosed species anticipate the instantly claimed invention is maintained for reasons made of record in the office action mailed 6-16-04.

Applicants' arguments and amendments are noted but still do not obviate the rejection of record. The rejection is maintained for reasons made of record until all the claims are rendered allowable.

Claims 1-5, 9-14, 16-21 and 23 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained in part for reasons made of record.

Applicant arguments with respect to "S" are persuasive. Applicants arguments with regard to "F" are not. As to "F", F is specifically defined in the specification to indicate that allows secretion of a protein encoded by Y into a fermentation medium. In contrast to Applicants assertion, hirudin or it derivatives or variants have not been demonstrated to have this property, absent the presence of a heterologous signal sequence in the nucleic acid. This is specifically acknowledged by applicants and their reliance upon PCT/EP00/08537. Absent the signal sequence "S" to allow for secretion of the hiruidin protein into a fermentation medium, hirudin will not be secreted. Therefore "F" which applicants define in the specification as a sequence allowing secretion of "Y" cannot be hirudin because there is no evidence of record the hirudin *per se* allows secretion of a protein into the fermentation medium. The sequence of the prior art that allows secretion of hirudin into the fermentation medium is the signal sequence not the hirudin sequence. Every single Example of the specification and the art from which the plasmids were derived and which Applicants rely upon have signal sequences to allow the hirudin protein to be secreted. It is not the hirudin sequence per se that allows secretion. This specification fails to teach that hirudin per se, absent a 5' signal sequence has the functional property of allowing secretion of protein "Y". Applicants attempt to

functionally define hirudin as the nucleic acid sequence providing for "F" which is defined in the specification at page 11. There is no teaching in the specification that provides for an expression construct limited to hirudin or derivative thereof provides for secretion. In other words, hirudin or derivative thereof itself has not been demonstrated in any host cells to be recombinantly produced as a secreted product, absent more. Applicants argue that the specification at page 12 further defines "F" as hirudin. The examiner concedes that the specification defines "F" as encompassing hirudin. However, the specification does not teach that the nucleic acid encoding hirudin *per se* has the functional property of allowing secretion of "Y". In otherwords, the construct of claim 1 is incapable of producing a secreted protein product. The specification as filed, does not provide written description of the nucleic acid of claim 1, secreting a functional proinsulin or insulin. As such, hirudin per se does not meet Applicants own definition of "F" as set forth in the specification as filed. The specification as filed does not teach that hirudin per se allows the secretion of insulin as required by the definition of "F". Therefore, applicants were not in possession of "F" as it relates to a hirudin that functions to allow secretion of "Y". There is no showing of record that any hirudin has that additional defined property of "F" as set forth in the specification as filed. The issue is "F" *alone* does not provide for the function as set forth in the specification. All Applicants arguments rely upon the presence of "S" for secretion of the fusion protein. Applicants argue the definition of allow and try to rely upon different definitions of allow to provide for a broader definition. This is not persuasive, Applicants use the word allow in the specification and as construed by one of skill in the art, this would mean that the sequence necessarily provides for that property. Applicants contort the meaning to provide for some alleged functionality that is not demonstrated, that hirudin alone as claimed allows for/permits secretion. This is a necessary property of "F" as defined in the specification. Applicants argue many components are required for secretion and that the combination allows for secretion and any one component cannot alone provide for the process. If this is true, then Applicants'

invention is not fully described because it does not define the full scope of the elements that are required to "allow" secretion. The issue is "F" allowing secretion. In view of the teachings of the specification, hirudin alone does not allow secretion, it is merely that simple. The construct of claim 1 has not been demonstrated in any prokaryotic or eukaryotic cell to provide for a secreted protein product. Applicants arguments are not persuasive.

The "F" issue may be resolved by applicants amending the claims 1 and 2 to recite -Hir-As-Rn-Y- and indicate that Hir is hirudin.

Claim 1-5, 9-14, 16-21 and 23 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the particularly disclosed nucleic acids encoding fusion proteins, plasmids, bacterial host cells and methods of fermentative production in a bacterial cell and isolation of the fusion proteins thereof from a culture supernatant as particularly set forth in the Examples of 1-9 of the specification, it does not reasonably provide enablement for the claimed nucleic acids encoding fusion proteins, plasmids, host cells, methods of making and purification is maintained for reasons made of record.

Applicants' arguments are not persuasive with respect to the issue of hirudin as allowing for or directing secretion into a culture cell medium and isolation from a supernatant (i.e. the "F" issue). All of the examples provide for a particular nucleic acid, a particular signal sequence and defined host cell (*E. coli*) to get production into the culture medium. Further as previously discussed, there is no evidence of record that the nucleic acid of claim 1 is either expressed or secreted as is even when integrated into the host cell chromosome, absent a promoter and signal sequence. Applicants have simply not provided any evidence of such in any of the relied upon Examples. As such, this rejection is maintained, as Applicants have not particularly overcome these issues.

Applicants arguments with respect to the scope of hirudin is persuasive because applicants have several naturally occurring and several variants that provide for description of a hirudin genus and this part of the rejection is withdrawn.

Amendment of claims 1 and 2 to recite -Hir-As-Rn-Y- and indicate that Hir is hirudin would obviate the "F" issue. With respect to host cells and production of the protein , these claims must be dependent from claim 2, because fermentative secretion (i.e. into the fermentation medium/broth/supernatant from a heterologous host cell requires a nucleic acid construct with a promoter and a signal sequence.

Claims 3, 4, 5 and 21 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons made of record.

As to claim 3, the following phrases have no meaningful interpretation "smompa derived from", "ecoompc derived from", "af009352 derived from", "aeoynxa derived from" or "stomps1 derived from" because these acronyms apparently represent specifically claimed nucleic acid sequences not described nor specifically defined in the specification is maintained for reasons made of record. Applicants argue that the definitions are not intended to limit the claims. However, the words or acronyms are intended to limit the claims. These two positions are completely opposite. Either a phrase limits to a particular sequence or it does not. As such, the sequences represented by the acronyms are not clearly and unambiguously defined in the specification or the claims sufficient to allow the skilled artisan to determine when they are infringing or not. It is suggested that Applicants use simpler language such as that recited for the first alternative "the signal sequence of the oprF gene from *Pseudomonas fluorescens*" and delete the references to the acronyms since they have been argued on one hand to define a sequence and on the other hand not. If the acronyms are intended to represent a particular nucleic acid sequence, then it appears that this is an improper incorporation by reference. A search of

the non-patent literature does not define these acronyms and as such the metes and bounds cannot be readily ascertained.

As to claim 4, Applicants' arguments are not fully persuasive. Applicants argue that Ser-hirudin or Ala-hirudin are conventional names for the N-terminal substitutions of the art for known commercially available variants. This would be persuasive in view of the presented evidence, however, Applicants now indicate that the hirudin that carries serine or alanine instead of leucine at position 1 of the amino acid sequence as now recited in claim 5 , appears to further limit Ser-hirudin or Ala-hirudin of claim 4. Therefore, the argued position of conventional terminology is in seeming contrast to the amendment of claim 5 to further define the position of serine or alanine. Did Applicants intend also to amend claim 4 instead ?

Status of Claims

All claims stand rejected.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-Th 6:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patricia A. Duffy
Primary Examiner
Art Unit 1645